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## **A Role of AKAP5 in PKA and Epac Mediated PKB/Akt Phosphorylation in the Lung.**

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Protein kinase B (PKB)/Akt is a key mediator of cell proliferation, cell survival and metabolism. Disbalance in PKB/Akt signaling occurs in inflammatory diseases including Alzheimer's dementia and chronic obstructive pulmonary disease.

While the strong connection of cAMP–dependent signaling with downstream PKB/Akt is established, the precise nature of this connection remains unknown. We reported recently that cAMP–dependent protein kinase (PKA) activation reduced PKB/Akt phosphorylation, whereas activation of Rap–specific exchange proteins directly activated by cAMP (Epac1 and Epac2) enhanced PKB/Akt phosphorylation in murine neurons. We show that PKA, PKB/Akt and Epac2 complex with neuronal A–kinase anchoring protein5 (AKAP5).

After establishing the opposite effects of the two cAMP effectors Epac and PKA on PKB/Akt phosphorylation in murine neurons, we investigated the role of cAMP on PKB/Akt phosphorylation in both HEK293 cells, which are known to exhibit human neuronal signaling capacities and in human airway smooth muscle (hTERT) cells.

Indeed, activation of PKA reduced PKB/Akt phosphorylation, whereas activation of Epac proteins increased PKB/Akt phosphorylation. Again we show that PKA, PKB/Akt and Epac complex with AKAP5. In such multiprotein complexes, differences in amounts of bound PKA and Epac proteins can modulate PKB/Akt phosphorylation, as shown in our studies with Epac1 and Epac2 specific siRNAs and cell treatment with peptides disrupting PKA anchoring to AKAPs.

The involvement of Akt–related phosphatases is currently under investigation. We conclude that AKAP5 acts as a key regulator balancing the two cAMP pathways in PKB/Akt phosphorylation in neuronal and lung cells.

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